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Self-Recognition in the Coordination-Driven Self-Assembly of Three-Dimensional M_3L_2 Polyhedra

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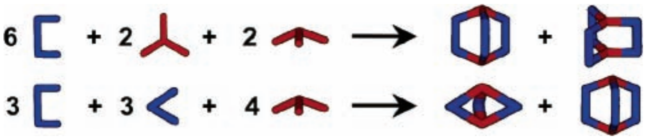
ABSTRACT



Self-recognition in the coordination-driven self-assembly of three-dimensional (3-D) polyhedra is described. Multiple discrete 3-D polyhedra were formed in one vessel through the self-recognition of a mixture of subunits. The dynamic self-recognition process is determined by the information stored within the geometry and directionality of multiple rigid building blocks as well as the thermodynamic stability of the discrete products.

Self-recognition and self-selection, whereby complementary molecular or macromolecular components are able to self-organize according to the specific information encoded within their individual structures, are critical phenomena in biological systems. Over time, self-recognition and selection allow for functional, higher order macromolecules to emerge from complex, multicomponent mixtures by virtue of dynamic self-assembly. The enormous amount of information stored within DNA and RNA, for example, can be retrieved and processed because of the noncovalent hydrogen bond promoted self-recognition and self-selection that occur between relatively few nucleic acid bases. Higher level polyhedral assembly can be seen in the proteasome of the yeast *Saccharomyces cerevisiae*, which is composed of pairs of seven different protein building blocks self-assembled into a C_7-symmetric structure.[1] With the aim of obtaining valuable insight into Nature's own self-recognition process, the formation of discrete molecular architectures from the noncovalent self-assembly of multiple subunits has been extensively explored for over a decade.[2−17]

The processes of self-recognition and self-selection are influenced by the steric, geometric, and electronic information embedded within each individual molecular component. Noncovalent interactions (e.g., hydrogen bonding, metal−ligand coordination, donor−acceptor interactions, etc.) can be used to promote the recognition and self-assembly of those

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(1) Groll, M.; Dizel, L.; Löwe, J.; Stock, D.; Bochter, M.; Bartunik, H. D.; Huber, R. *Nature* **1997**, *386*, 463−471.
(2) Lehn, J.-M. *Angew. Chem., Int. Ed.* **1990**, *29*, 1304−1319.
(3) Lehn, J.-M. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4763−4768.
(4) Nitschke, J. R. *Acc. Chem. Res.* **2007**, *40*, 103−112.
(5) Masood, M. A.; Enemark, E. J.; Stack, T. D. P. *Angew. Chem., Int. Ed.* **1998**, *37*, 928−931.
(6) Enemark, E. J.; Stack, T. D. P. *Angew. Chem., Int. Ed.* **1998**, *37*, 932−5.
(7) Albrecht, M.; Schneider, M.; Röttele, H. *Angew. Chem., Int. Ed.* **1999**, *38*, 557−559.
(8) Kim, T. W.; Lah, M. S.; Hong, J.-I. *Chem. Commun.* **2001**, 743−744.
(9) Shi, X.; Fettinger, J. C.; Davis, J. T. *J. Am. Chem. Soc.* **2001**, *123*, 6738−6739.
(10) Albrecht, M.; Schneider, M. *Eur. J. Inorg. Chem.* **2002**, 1301−1306.
(11) Isaacs, L.; Witt, D. *Angew. Chem., Int. Ed.* **2002**, *41*, 1905−1907.
(12) Lehn, J.-M. *Science* **2002**, *295*, 2400−2403.
(13) Kobayashi, K.; Yamada, Y.; Yamanaka, M.; Sei, Y.; Yamaguch, K. *J. Am. Chem. Soc.* **2004**, *126*, 13896−13897.
(14) Hori, A.; Yamashita, K.-I.; Fujita, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 5016−5019.
(15) Schultz, D.; Nitschke, J. R. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 4763−4768.
(16) Schmittel, M.; Kalsan, V.; Kishore, R. S. K.; Cölfen, H.; Bats, J. W. *J. Am. Chem. Soc.* **2005**, *127*, 11544−11545.
(17) Schultz, D.; Nitschke, J. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 2453−2456.

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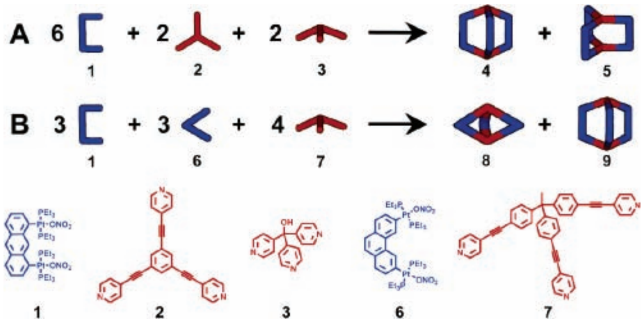
components that possess complementary structural information while mismatched components do not recognize each other. The dynamic nature of noncovalent interactions ensures that less stable kinetic combinations of complementary subunits can continuously reassemble to form, over time, the most thermodynamically stable product(s). In cases when only two complementary molecules are mixed, the self-assembly process may proceed quickly to produce one product. When many complementary subunits are mixed, dynamic self-assembly allows for two or more discrete products to emerge from the complex mixture on account of self-recognition and self-selection of the most thermodynamically stable assemblies.

For example, in 1993, Lehn et al. demonstrated[18] that complex multicomponent mixtures of oligobipyridine strands, differing in length, will self-recognize and self-assemble in the presence of Cu^{I} and Ni^{II} ions into well-defined double and triple helicates. Self-recognition and assembly of the different helicate products was dependent upon the length of the strands, their structure, and the preferred coordination geometry of the metal ions.[18] Raymond et al. later observed[19] another self-recognition phenomena where product formation is determined by the distance between two coordination sites of different ligands during the self-assembly of triple-stranded homoleptic helicates. The great deal of literature on self-recognition in the self-assembly of helicates, however, contrasts to that of one of the most prominent three-dimensional (3-D) architectures, polyhedra, where literature reports have proven to be surprisingly rare.[20]

Recently, we have reported that multicomponent mixtures of two and three organoplatinum donors and a 4,4′-dipyridyl acceptor undergo self-recognition to give multiple, discrete two-dimensional polygons as dominant products.[21] Considering that the self-assembly of discrete supramolecular structures is always in competition with oligomerization, extending these 2-D studies of polygons to the self-assembly of 3-D polyhedra will likely be more challenging. The building blocks suitable for 3-D polyhedra contain not only additional binding sites but also a greater variety of bonding angles, and thus, the self-assembly of polyhedra is in competition with a much greater number of both linear and nonlinear oligomers, resulting in an enormous number of different multicomponent topologies.

According to the "directional bonding" model,[22−23] discrete 3-D cages of the type M_3L_2 can be rationally assembled[24−26] using both planar[25] (**2** in Scheme 1) and *non*planar[24] (Scheme 1, **3** and **7**) tritopic donors when combined with di-Pt(II) acceptors, such as a 0° "clip"[24,25] or 60° angular building block[26] (**1** and **6**, respectively, in Scheme 1). It is most often the case that complementary building blocks are mixed only in stoichiometric ratios that favor the formation of one desired product and disfavor the formation of undesired byproducts. A more complex situation in self-assembly arises when multiple different subunits are mixed together in one pot. The question arises: will the geometric and directional information encoded in the different building blocks be enough to overcome the intrinsic disorder of a complex mixture in order to produce a highly ordered system of discrete polyhedra in solution? Herein, we present an investigation of self-recognition in the self-assembly of 3-D polyhedra from multiple components (Scheme 1). Despite the possibility of forming myriad oligomeric structures, we demonstrate that the discrete, highly symmetric M_3L_2 cages are strongly preferred and the information encoded within binding units is preserved.

Scheme 1. Graphical Representation of Self-Recognition in the Coordination-Driven Self-Assembly of 3-D Polyhedra



When molecular clip **1** is mixed with planar and *non*planar tritopic tectons **2** and **3** in a 3:1:1 ratio and heated at 55 °C for 48 h in aqueous acetone (v/v 1/1), distorted trigonal prism[23] (DTP) **4** and nondistorted trigonal prism[24] (NTP) **5** are the main products formed (Scheme 1A). The self-assembly process was monitored using multinuclear NMR spectroscopy (^1H and ^{31}P).

After 6 h, the ^{31}P $\{^1H\}$ NMR spectrum of the reaction mixture shows intense peaks at δ 9.7 ppm (DTP **4**) and 8.6 ppm (NTP **5**), flanked by unassignable resonances that are representative of intermediate byproducts (Figure 1a). Likewise, some signals in the ^1H NMR spectrum can be assigned to cages **4** and **5** (e.g., $\delta = 9.41$ ppm, H_9 in NTP **5**; $\delta = 9.13$ ppm, $H_{\alpha-Py}$ in DTP **4**), though broad peaks and unassignable signals, indicative of oligomeric structures, are also observed (Figure 2a). After 48 h, the unassignable resonances in the ^{31}P $\{^1H\}$ NMR and ^1H NMR spectra disappear (Figures 1c and 2c); the ^{31}P $\{^1H\}$ NMR spectrum indicates only two dominant Pt species, and the ^1H NMR spectra simplifies drastically with sharp signals that correlate well to discrete polyhedra **4** and **5** despite some peak overlap.

Anion exchange with KPF_6 affords the assemblies as hexafluorophosphate salts, the ESI mass spectrum of which is

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[18] Krämer, R.; Lehn, J.-M.; Marquis-Rigault, A. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *99*, 5394−5398.

[19] Caulder, D. L.; Raymond, K. N. *Angew. Chem., Int. Ed.* **1997**, *36*, 1440−1442.

[20] Ziegler, M.; Miranda, J. J.; Andersen, U. N.; Raymond, K. N. *Angew. Chem., Int. Ed.* **2001**, *40*, 733−736.

[21] Addicott, C.; Das, N.; Stang, P. J. *Inorg. Chem.* **2004**, *43*, 5335−5338.

[22] Seidel, S. R.; Stang, P. J. *Acc. Chem. Res.* **2002**, *35*, 972−983.

[23] Leininger, S.; Olenyuk, B.; Stang, P. J. *Chem. Rev.* **2000**, *100*, 853−908.

[24] Kuehl, C. J.; Kryschenko, Y. K.; Radhakrishnan, U.; Seidel, S. R.; Huang, S. D.; Stang, P. J. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4932−4936.

[25] Kuehl, C. J.; Yamamoto, T.; Seidel, S. R.; Stang, P. J. *Org. Lett.* **2002**, *4*, 913−915.

[26] Yang, H.-B.; Ghosh, K.; Arif, A. M.; Stang, P. J. *J. Org. Chem.* **2006**, *71*, 9464−9469.

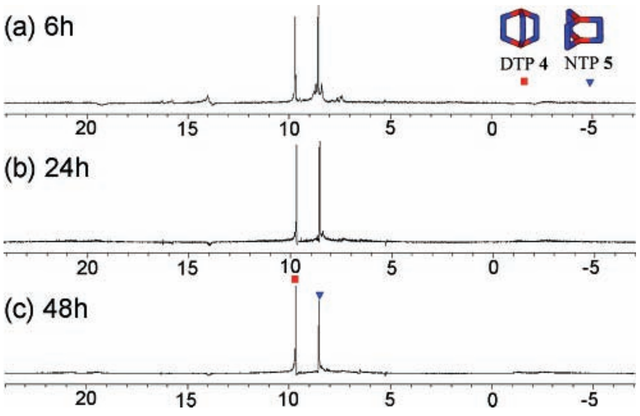

Figure 1. $^{31}P\{^1H\}$ NMR spectra (acetone-d_6/D_2O 1/1) recorded between 6 and 48 h during the formation of DTP **4** and NTP **5**.

shown in Figure 3. The ESI mass peaks at $m/z = 2069.8$ and 1331.4, corresponding to the [DTP (**4**) $-$ $2PF_6]^{2+}$ and [DTP (**4**) $-$ $3PF_6]^{3+}$ species, are found. Two additional charged states at m/z=1437.8 and 1042.4, which correspond to the species [NTP (**5**) $-$ $3PF_6]^{3+}$ and [NTP (**5**) $-$ $4PF_6]^{4+}$, are also observed. These peaks were isotopically resolved and agree very well with the theoretical distribution as shown in Figure 4.

All NMR and ESI spectroscopic results indicate that self-recognition during the self-assembly of 3-D cages from a complex mixture of di-Pt(II) acceptor **1** and different tritopic donors **2** and **3** provides two discrete prisms and with no significant observable byproducts. In order to study the scope of this new self-recognition process, it is necessary to investigate the same self-assembly process in reverse by mixing tritopic donor **7** and different di-Pt(II) acceptors **1** and **6** (Scheme 1B).

Heating 0° and 60° di-Pt(II) acceptors **1** and **6**, respectively, and nonplanar tritopic donor **7** in a 3:3:4 ratio at 55 °C for 72 h in aqueous acetone (v/v 1/1) results in trigonal-bipyramid[25] (TBP) **8** and distorted trigonal prism[23] (DTP) **9** as major products. Multinuclear NMR spectroscopy (^1H and ^{31}P) was used to follow the self-assembly process. After 6 h, two broad peaks along with a number of lower intensity signals are observed in the ^{31}P $\{^1H\}$ NMR spectrum (Figure 5a). Likewise, the ^1H NMR spectrum displays broad resonances resulting from the initial generation of oligomers (Figure 6a). Upon extended heating, the broad peaks in both ^{31}P $\{^1H\}$ NMR and ^1H NMR spectra (Figures 5d and 6d) become well-resolved and unassignable resonances slowly disappear, indicative of the formation of discrete, highly symmetric 3-D cages TBP (**8**) and DTP (**9**).

Following anion exchange with KPF_6, ESI mass spectrometry provided further evidence of the formation of discrete TBP **8** and DTP **9** in one vessel. 3-D cages TBP **8** and DTP **9** have the same molecular formula ($C_{196}H_{258}F_{36}P_{18}Pt_6N_6$), therefore only one set of signals is observed in the ESI mass spectrum. Spectral results showed three charged

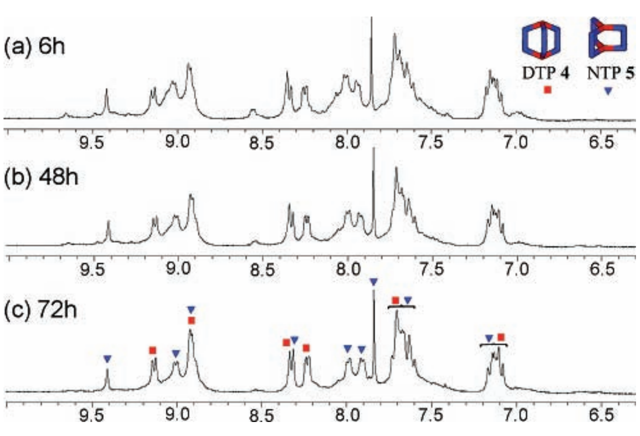

Figure 2. ^1H NMR spectra (acetone-d_6/D_2O 1/1) recorded at various time intervals during the formation of **4** and **5**.

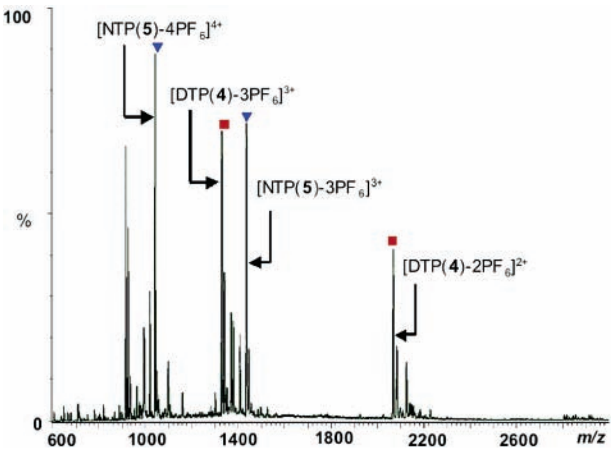

Figure 3. Full ESI mass spectrum of product mixture DTP **4** and NTP **5**.

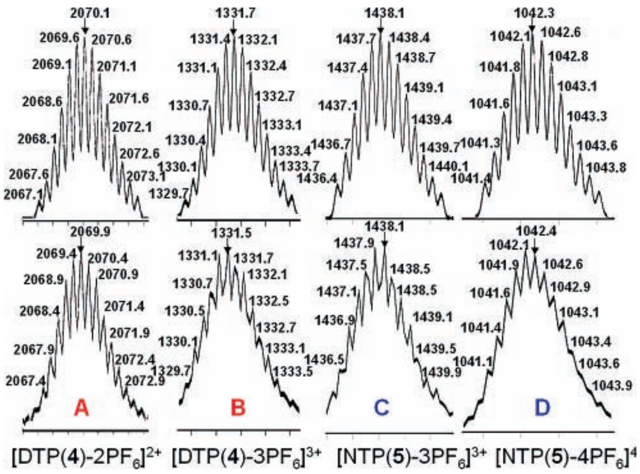

Figure 4. Calculated (top) and experimental (bottom) ESI-MS spectra of DTP **4** (A and B) and NTP **5** (C and D).

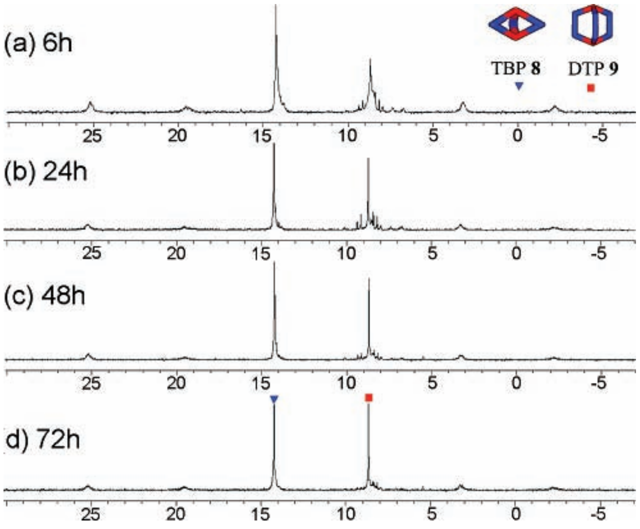

Figure 5. $^{31}P\{^1H\}$ NMR spectra (acetone-d_6/D_2O 1/1) recorded between 6 and 72 h during the formation of TBP **8** and DTP **9**.

states at $m/z = 2408.7$, 1557.5, and 1131.6, corresponding to $[M - 2\ PF_6]^{2+}$, $[M - 3\ PF_6]^{3+}$, and $[M - 4\ PF_6]^{4+}$, where M represents the intact assemblies, and their isotopic resolutions are in excellent agreement with the theoretical distributions (see the Supporting Information).

We have described the formation of discrete 3-D polyhedra from multiple subunits in a complex mixture. The self-recognition process is strongly dependent upon the structural information stored within individual building blocks, i.e., geometry, directionality, and rigidity. As outlined in Scheme 1A, for example, the processing of information stored within the acceptor unit **1** through different algorithms prescribed by its interactions with planar and *non*planar donor subunits **2** and **3** allows for the self-recognition and organization of the two discrete output architectures DTP (**4**) and NTP (**5**). The result is a manifold expression of molecular information through "postinformational operation.[3]"

In addition, the thermodynamic stability of the products also plays a great role in the self-recognition process. In both cases, extended reaction times (48−72 h as compared with just 5−20 h in the cases of the individual cages[23−25]) are necessary for the formation of discrete 3-D polyhedra from multiple components, presumably because of the increased number of intermediate byproducts encountered during assembly. Self-recognition and self-assembly are achieved as the kinetically labile Pt−N bond allows for the dynamic exchange of complementary molecular components by internal rearrangement, exchange, extrusion, and incorporation of different components, through which intermediate assemblies are self-selected and proof-read in order to generate the most thermodynamically preferred 3-D cages.

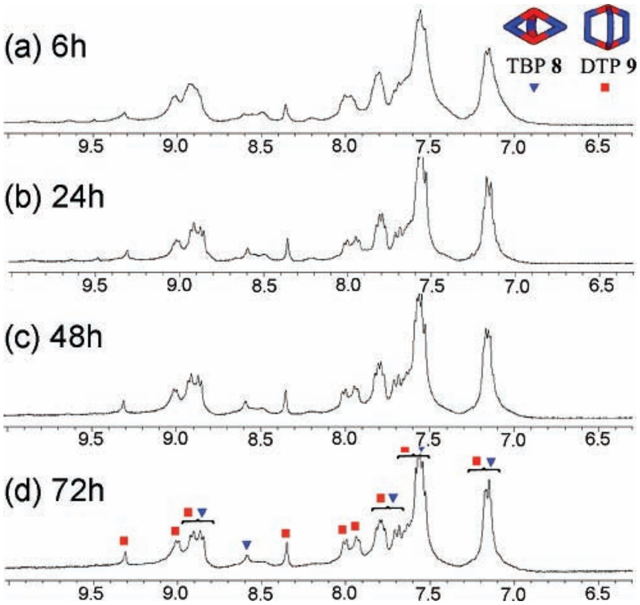

Figure 6. ^1H NMR spectra (acetone-d_6/D_2O 1/1) recorded at various time intervals during the formation of **8** and **9**.

In conclusion, these studies provide a new example of self-assembly as controlled by self-recognition and self-selection processes opperating in a complex mixture, once again proving the versatility and modularity of such processes in the formation of supramolecular architectures. These results help provide an enhanced understanding of the geometric and thermodynamic factors that influence self-assembly within multicomponent mixtures and have implications in the same processes that govern the assembly of higher order biological structures from even more complex mixtures in nature.

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Supporting Information Available: Experimental procedure and ESI mass spectrum of product mixture TBP **8** and DTP **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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